

## DESCRIPTION

## REDUCED COENZYME Q-CONTAINING COMPOSITION

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## TECHNICAL FIELD

This invention relates to the provision, as a material for use in foods, functional foods, drugs or quasidrugs, of a reduced coenzyme Q-containing composition which is excellent in solubility or dispersibility in water and in storage stability in spite of the nonuse of any of those natural emulsifiers or synthetic emulsifiers and/or liposomes which are in general and frequent use.

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## BACKGROUND ART

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Coenzymes Q are essential constituents widely distributed in living bodies, from bacteria to mammals and are known as mitochondrial electron transfer system constituents in cells of living bodies. Through repeated oxidation and reduction in mitochondria, coenzymes Q perform their function as transmitter components in the electron transfer system and, further, reduced coenzymes Q are known to have antioxidant activity. In humans, coenzyme Q<sub>10</sub>, whose coenzyme Q side chain comprises 10 repeating structures, is the main component and, generally, about 40 to 90% thereof occurs in reduced form in living bodies. The physiological activities of coenzymes Q may be energy production activation through mitochondrial activation, cardiac function activation, cell membrane stabilizing effect, and cell protecting effect through antioxidant activity.

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Coenzymes Q are known to be useful in various application fields. For example, oxidized coenzyme Q<sub>10</sub> is used as a remedy for congestive heart failure owing to its effects on the heart. Besides such medical uses, they are orally used as nutrients or nutritional supplements, like

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vitamins, in the form of supplements or health drinks.

In recent years, various reports have been published about the aggravation of diseases due to increases in oxidative stress in blood. Typical examples are arteriosclerosis, complications of diabetes and the like diseases. These diseases are caused and/or aggravated by denaturation of lipids and the like due to various oxidative stresses occurring in blood. For counteracting such effects of oxidative stresses, antioxidant activity promotion in living bodies by administration of an antioxidant is effective. Vitamin E is a compound representative of the liposoluble antioxidants considered to be more effective in inhibiting lipid peroxidation and is in wide use as antioxidants in disease prevention and so on. On the other hand, it has been reported that the coexistence of reduced coenzyme Q<sub>10</sub> is important for vitamin E to properly perform its antioxidant activity (Bowry et al., 1993, J. American Chemical Society, 115, 6029-6044), and the importance of coenzymes Q, together with vitamin E, as liposoluble antioxidant substances is becoming clear.

Coenzymes Q have themselves strong antioxidant activity and, therefore, the antioxidant activity in blood can be effectively enhanced by sending a sufficient amount of reduced coenzymes Q in solubilized form into blood.

The enhanced antioxidant activity in blood is considered to be useful widely in preventing vascular lesions during ischemia-reperfusion, preventing restenosis in arteriosclerosis, preventing vascular lesions following cerebral infarction, preventing arteriosclerosis, preventing complications of diabetes, and preventing a number of other diseases from being aggravated supposedly by active oxygen species.

Furthermore, by sending it into the living body in a new delivery form, namely by drip, it becomes possible to

provide patients with a serious illness or a brain disease, who are incapable of oral intake, with coenzymes Q. It is thus expected that solubilization of coenzymes Q will bring about a number of merits.

5       As is well known, coenzymes Q can occur in both the oxidized form and reduced form, and a number of investigations have so far been made about the method for solubilizing oxidized coenzyme Q<sub>10</sub> (also called as  
10       ubidecarenone or ubiquinone). As for the solubilization of oxidized coenzyme Q<sub>10</sub>, various methods have been reported, for example coating with liposomes, suspension using a surfactant or an oil and fat, and the like (for example Japanese Kokai Publication Hei-05-186340, Japanese Kokai Publication Hei-07-69874, Japanese Kohyo Publication 2000-  
15       510841).

      It is necessary for oxidized coenzyme Q<sub>10</sub> to be converted to reduced coenzyme Q<sub>10</sub> by the action of a reductase or the like in order to perform its antioxidant activity. Supposedly, oxidized coenzyme Q<sub>10</sub> taken orally is  
20       converted in vivo to reduced coenzyme Q<sub>10</sub> by means of NADPH-CoQ reductase, lipoamide dehydrogenase, thioredoxin reductase or the like to show antioxidant activity. However, there is also a fear of decrease, with aging, in the ability of such reductases and other enzymes occurring  
25       in vivo to reduce oxidized coenzyme Q<sub>10</sub> to reduced coenzyme Q<sub>10</sub>. Therefore, it is of significance to administer reduced coenzyme Q<sub>10</sub> from outside the body to the aged or those showing decreased oxidized coenzyme Q<sub>10</sub> reducing activity.

      Reduced coenzyme Q<sub>10</sub> itself has antioxidant activity,  
30       hence it is a substance much expected to be of great utility in the prevention/treatment of such diseases as mentioned above. However, reduced coenzyme Q<sub>10</sub> is an extremely unstable substance with respect to its physical property, and is auto-oxidized when it is exposed to air  
35       and moreover hardly dissolves in water. Therefore, reduced

coenzyme Q<sub>10</sub> has not been put into industrial use before.

Although a search report describing the preparation of reduced coenzyme Q<sub>10</sub> as a liposome-coated preparation for the purpose of studying oxidoreductases and the like is available (Kishi et al., 1999, BioFactors, 10, 131-138), the liposomes used were prepared extemporaneously in each experiment. Any method for stably solubilizing reduced coenzymes Q has not been known at all.

As a result of the intensive investigations previously made by the inventors, methods for preparing and storing liquid compositions in which reduced coenzyme Q<sub>10</sub> solubilized in water can be stably maintained could be found out (Japanese Kokai Publication 2003-026625, Japanese Kokai Publication 2003-119126). These inventions have made it possible to provide highly useful liquid compositions containing a reduced coenzyme Q solubilized in water to practical use. The present invention is an extension to those previous inventions and has the object to solubilize reduced coenzyme Q<sub>10</sub> in water and, at the same time, further improve the storage stability thereof.

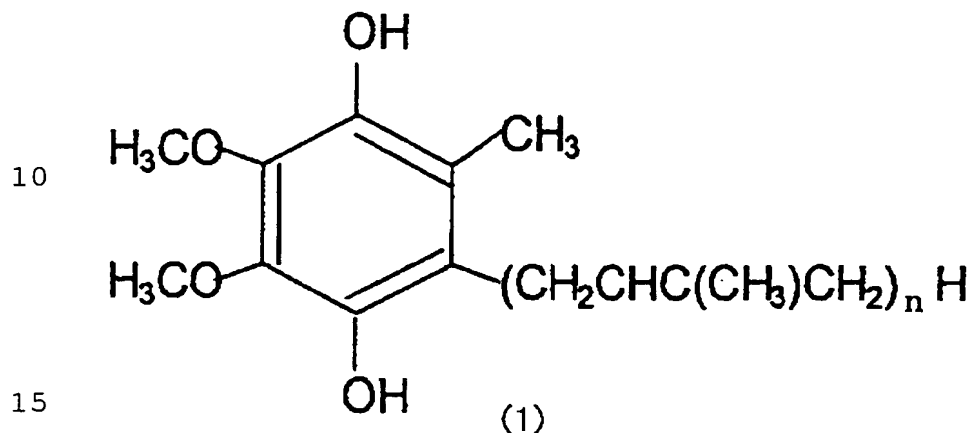
#### SUMMARY OF THE INVENTION

It is an object of the present invention to provide a composition containing a reduced coenzyme Q, which is a compound very unstable and poor in solubility or dispersibility in water, showing good solubility or dispersibility in water and capable of being stored at room temperature for a prolonged period of time.

The present inventors made intensive investigations to accomplish the above object and, as a result, found that the coexistence of a reduced coenzyme Q with a cyclodextrin results in marked improvement in storage stability and at the same time gives a composition having good dispersibility in water in spite of the fact that the reduced coenzyme Q is physically very unstable and almost

insoluble in water. Such findings have now led to completion of the present invention.

Thus, the present invention relates to a composition containing a cyclodextrin, a polar solvent and a reduced coenzyme Q represented by the general formula (1);



(in the formula, n is an integer of 1 to 12); wherein the reduced coenzyme Q is solubilized in said composition.

20 Further, the invention relates to a method for solubilizing a reduced coenzyme Q which comprises mixing a cyclodextrin, a polar solvent and a reduced coenzyme Q represented by the formula (1) given above.

25 The invention also relates to a method for producing a composition containing a cyclodextrin, a polar solvent and a reduced coenzyme Q, wherein the reduced coenzyme Q is solubilized in said composition, which method comprises mixing the cyclodextrin, the polar solvent and the coenzyme Q represented by the general formula (1) given above.

30 The invention further relates to a method for stabilizing a reduced coenzyme Q which comprises mixing a cyclodextrin, a polar solvent and a reduced coenzyme Q represented by the general formula (1) given above.

35 The invention still further relates to a method for inhibiting the oxidation of a reduced coenzyme Q which

comprises mixing a cyclodextrin, a polar solvent and the reduced coenzyme Q represented by the general formula (1) given above.

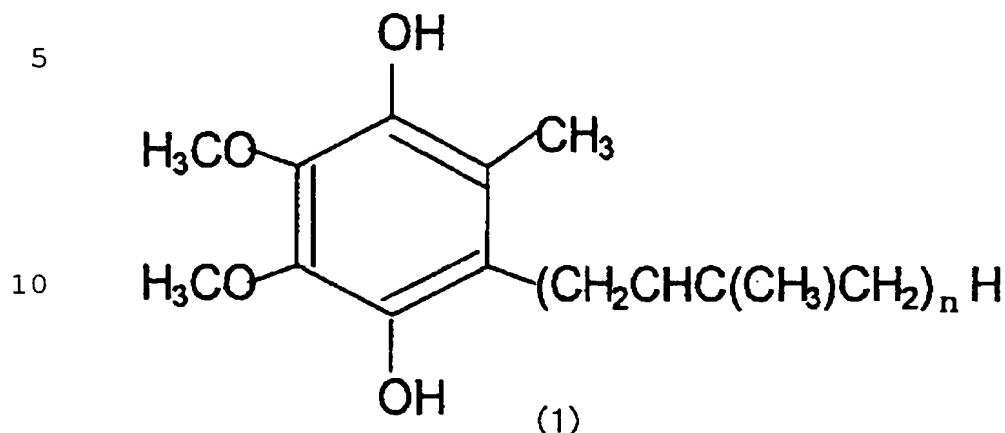
5                    DETAILED DESCRIPTION OF THE INVENTION

First, the composition of the invention which contains a cyclodextrin, a polar solvent and a reduced coenzyme Q, wherein the reduced coenzyme Q is solubilized in said composition, is described. The term "solubilized"  
10 is used herein to indicate that the coenzyme Q in question is dissolved in the composition mentioned above and the whole or a part of the coenzyme Q is clathrated in the cyclodextrin. The above composition may contain the part of the coenzyme Q which remains undissolved in the  
15 composition but is dispersed therein. The term "dispersed" is used herein to indicate that when the composition is subjected to the test described below, the coenzyme Q in the composition neither rises to the surface nor precipitates. The term "clathrated" is used herein to  
20 indicate a state of association of molecules constituting the composition so as to allow the coenzyme Q-containing composition to dissolve in water.

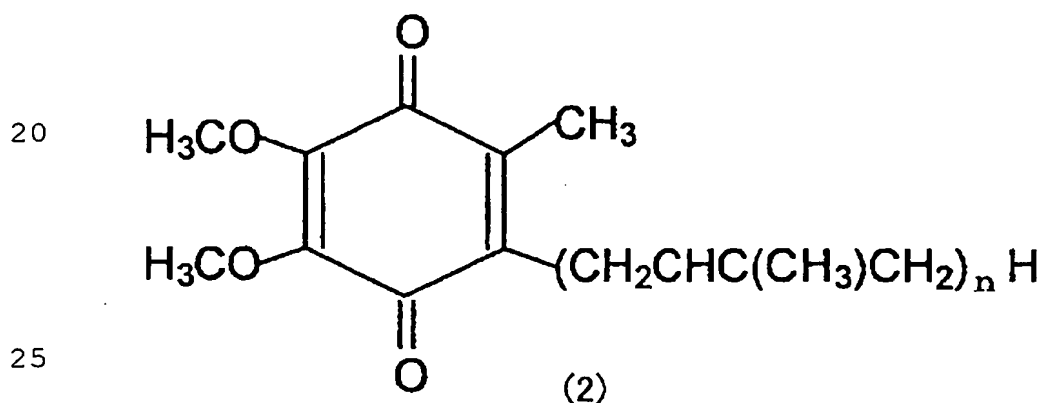
Whether a reduced coenzyme Q is solubilized in the above composition or not can be judged by the following  
25 test. Thus, 1 g of the composition is suspended in 500 ml of water and, after a lapse of 24 hours at 20°C, the suspension is observed by the eye. When a state of uniform dispersion can be confirmed, it is judged that the reduced coenzyme Q is in a solubilized state. Whether a reduced  
30 coenzyme Q is clathrated in a cyclodextrin or not can be judged by the following test. Thus, 1 g of the composition is suspended in 500 ml of water and, after a lapse of 24 hours at 20°C, the suspension is observed by the eye. When a state of uniform dispersion and a transparent solution  
35 state can be confirmed, it is judged that the reduced

coenzyme Q is clathrated in the cyclodextrin.

Coenzymes Q are represented by the formula (1);



15 (in the formula, n represents an integer of 1 to 12); and  
by the formula (2);



(in the formula, n represents an integer of 1 to 12); and  
the formula (1) represents reduced coenzymes Q and the  
formula (2) represents oxidized coenzymes Q. A reduced  
30 coenzyme Q may be crystalline or noncrystalline.

The composition of the invention may contain an  
oxidized coenzyme Q. When it contains both an oxidized  
coenzyme Q and a reduced coenzyme Q, the proportion of the  
reduced coenzyme Q to the total amount of the coenzymes Q  
35 (the sum of the oxidized coenzyme Q and the reduced

coenzyme Q) is preferably not smaller than 50% by weight, more preferably not smaller than 75% by weight.

The method for preparing the reduced coenzyme Q is not particularly restricted but, for example, the method comprising producing a coenzyme Q by any of the methods known in the art, for example by synthesis, fermentation, extraction from a natural source, and the like method and then concentrating the reduced coenzyme Q fraction in the eluate by chromatography can be employed. In this case, it is also possible to add a conventional reducing agent, such as sodium borohydride or sodium dithionite (hydrosulfite sodium), to the coenzyme Q if necessary and, after reduction of the oxidized coenzyme Q contained in the above coenzyme Q to a reduced coenzyme Q in the conventional manner, subject the reduction product to chromatography for concentration. It can also be obtained by the method comprising reacting a commercially available high-purity coenzyme Q with such a reducing agent as mentioned above.

The reduced coenzyme Q to be used in the present invention may be any of those in which the number (n in the formulas) of repeating units in the side chain is 1 to 12, as represented by the above formulas (1) and (2). However, the one having 10 repeating units in the side chain, namely reduced coenzyme Q<sub>10</sub>, can be used most adequately of all.

Cyclodextrin is not particularly restricted but, for example,  $\alpha$ -cyclodextrin,  $\beta$ -cyclodextrin,  $\gamma$ -cyclodextrin or the like can be used. Preferably the one selected from  $\alpha$ -cyclodextrin and  $\gamma$ -cyclodextrin is used. More preferably  $\gamma$ -cyclodextrin is used.

A proportion of a cyclodextrin contained is preferably 0.1 to 100 mole, and more preferably 0.2 to 20 mole, per 1 mole of a reduced coenzyme Q.

The term "polar solvent" is used herein to indicate water or alcohols. The polar solvent contained is not particularly restricted but includes water and alcohols



such as ethanol. These may be used singly or in combination thereof. A mixed solution containing water and ethanol is preferably used and water is more preferably used.

5 A proportion of a reduced coenzyme Q to a polar solvent is not particularly restricted. However, the usage of a reduced coenzyme Q to a polar solvent is usually 0.001 to 500 % by weight.

10 The composition of the invention which contains a reduced coenzyme Q in a solubilized form may contain an antioxidant. The antioxidant may be any compound having antioxidant activity and preferably comprises one or a mixture of two or more selected from citric acid, citric acid derivatives, vitamin C (ascorbic acid), vitamin C  
15 derivatives, vitamin E, vitamin E derivatives, glutathione, reduced glutathione, sodium thiosulfate, L-cysteine, L-carnitine, lycopene, riboflavin, curcuminoids, superoxide dismutase (SOD) and PQQ (pyrroloquinoline quinone). Furthermore, one or a mixture of two or more selected from  
20 citric acid, citric acid derivatives, vitamin C (ascorbic acid), vitamin C derivatives, vitamin E and vitamin E derivatives is more preferably used. The antioxidant to be contained is used preferably in an amount of not smaller than 0.01 mole but not greater than 1000 moles, more  
25 preferably not smaller than 0.1 mole but not greater than 100 moles, per 1 mole of a reduced coenzyme Q.

Now, a method for solubilizing a reduced coenzyme Q according to the invention is described. As the method of solubilization, there may be mentioned, for example, the  
30 method comprising bringing a reduced coenzyme Q into contact with a cyclodextrin, or mixing them together, in an appropriate polar solvent. Upon such contacting or mixing, a clathrate compound can be obtained. On the occasion of contacting or mixing, vigorous stirring of raw materials is  
35 preferred from the viewpoint of reduction of the time

required for clathrate formation. This is made for securing sufficient contact between a reduced coenzyme Q and a cyclodextrin. The conditions of vigorous stirring so referred to herein are, for example, as follows: 10 minutes  
5 of treatment at room temperature (about 20°C) at 20,000 rpm using a homomixer (Polytron PT2100).

As the polar solvent, there may be mentioned the same ones as mentioned hereinabove for the composition, for example, water and alcohols such as ethanol. These may be  
10 used in admixture. A mixture of water and ethanol is preferred, and water is more preferred. A reduced coenzyme Q may be used as such or in the form of a solution in a nonpolar solvent or a fat or oil.

Usable as the nonpolar solvent are, for example,  
15 hexane, ethers, and oils and fats. Preferred as the oils and fats are olive oil, perilla oil, rapeseed oil, rice bran oil, soybean oil, fish oil and the like since they are edible. These may be used in combination. The cyclodextrin may be used in the form of a solution in a  
20 polar solvent or as such.

The order of mixing the reduced coenzyme Q, the cyclodextrin and the polar solvent is not particularly restricted. Preferably, however, the cyclodextrin is dissolved in the polar solvent, and the reduced coenzyme Q  
25 is then added to the solution for contacting and mixing up. More preferred is a procedure comprising dissolving the cyclodextrin in the polar solvent and simultaneously adding the reduced coenzyme Q for contacting and mixing up. In these procedures, the reduced coenzyme Q is clathrated by  
30 the cyclodextrin and a clathrate compound is formed. In this way, a composition containing a reduced coenzyme Q solubilized and soluble or uniformly dispersible in water is obtained.

The order of mixing the reduced coenzyme Q, the  
35 cyclodextrin, the polar solvent and the antioxidant is not

particularly restricted. For example, it is possible to dissolve the antioxidant in the polar solvent, add the cyclodextrin to the solution and, thereafter, add the reduced coenzyme Q for contacting and mixing up.

5 Alternatively, it is also possible to add the cyclodextrin to the polar solvent, then add the reduced coenzyme Q for contacting and mixing up and, thereafter, add the antioxidant. The antioxidant may be used either as such or in the form of a solution in the above-mentioned polar  
10 solvent.

The compositions containing a reduced coenzyme Q solubilized by the method of solubilization all fall within the scope of the present invention.

A further description is now given of the method for  
15 producing a composition containing a cyclodextrin, a polar solvent and a reduced coenzyme Q represented by the formula (1) given hereinabove, wherein the reduced coenzyme Q is solubilized therein, which method comprises mixing the cyclodextrin, the polar solvent and the reduced coenzyme Q.  
20 In carrying out that method, a proportion between a reduced coenzyme Q and an oxidized coenzyme Q, other materials to be used, an order of feeding of materials, a proportion between a reduced coenzyme Q and a cyclodextrin and other conditions are the same as those described above referring  
25 to the method of solubilization.

The composition according to the invention can be subjected to spray drying, freeze-drying and the like to give a powdery composition. More preferably, the composition is to be obtained in the form of a powdery  
30 composition in view of the simplicity in practical handling and the ease of industrial utilization. In this way, a composition excellent in solubility or dispersibility in water and capable of being stored at room temperature or in a refrigerator for a long period of time can suitably be  
35 obtained.

The composition to be prepared may contain one or more of other pharmaceutically acceptable materials. The pharmaceutical materials that can be contained in the composition include, for example, colorants, emulsifiers, 5 tonicity adjusting agents, buffering agents, dissolution aids, preservatives, correctives, stabilizers, excipients and the like. The composition may further contain one or more of other active ingredients, for example, drugs, nutrient supplements and the like, according to the 10 intended use thereof. These pharmaceutical materials can be properly prepared in the conventional manner. The composition of the invention can be further subjected to granulation, for example, extrusion granulation, fluidized bed granulation or the like.

15 Further, the composition may contain one or more of various ingredients considered to be useful in maintaining the health of animals, including humans, pets, domestic animals and the like, for example, medicinal ingredients, functional food components, supplement components or the 20 like. These ingredients can be properly added in the conventional manner.

A dosage form of the composition obtained in accordance with the invention is not particularly restricted but can be adequately selected according to the 25 intended use thereof. In view of its good solubility or dispersibility in water, it is preferably used for oral administration.

The reduced coenzyme Q-containing composition of the invention can be used in foods, functional foods, drugs, 30 quasidrugs or the like for humans or animals. The term "functional foods" is used herein to indicate foods to be taken for health maintenance or for nutrition in lieu of taking meals, for example, health foods, dietary supplements, supplements, nutritious foods or the like. 35 More specific forms include, but are not limited to, health

drinks, chewable tablets, capsules, tablets, injections, transfusions, ophthalmic solutions, feeds or the like.

The solubilized composition obtained by the solubilizing method of the invention can stably maintain a reduced coenzyme Q against oxidation thereof. The term "can stably maintain" is used herein to indicate that when the solubilized composition is stored, in a state protected against light, in an air atmosphere at room temperature (about 20°C) for 4 weeks, the residual reduced coenzyme Q percentage as evaluated is not lower than 80% relative to the concentration at the time of starting storage, although the limit residual percentage may vary depending on the intended use or purpose of the composition and on the storage conditions.

Now, a description is given of the method for preventing the oxidation of a reduced coenzyme Q according to the invention which method comprises mixing a cyclodextrin, a polar solvent and a reduced coenzyme Q represented by the formula (1) given hereinabove. After 4 weeks of storage of a reduced coenzyme Q, in a state protected against light, in an air atmosphere at room temperature (about 20°C), when the residual reduced coenzyme Q percentage is not lower than 80% of the amount at the time of starting storage, the oxidation of the reduced coenzyme Q is judged to have been inhibited according to the method. In carrying out the method, such conditions as a proportion between a reduced coenzyme Q and an oxidized coenzyme Q, other materials to be used, and a proportion between a reduced coenzyme Q and a cyclodextrin are the same as in the case of the composition described above.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a graphic representation of the stability of reduced coenzyme Q<sub>10</sub> in each powdery composition against

autooxidation at 23°C. The ordinate denotes residual reduced coenzyme Q<sub>10</sub> percentage relative to total coenzyme Q<sub>10</sub> contained in the composition (test sample), and the abscissa denotes the number of storage days. At 4 weeks after starting storage, the bulk powder of reduced coenzyme Q<sub>10</sub> showed a decrease in the reduced coenzyme Q percentage to 41% whereas the reduced coenzyme Q percentage was not lower than 80% in all the powder compositions I-IV.

Fig. 2 is a graphic representation of the stability of reduced coenzyme Q<sub>10</sub> in each powdery composition against autooxidation at 40°C. The ordinate denotes the residual reduced coenzyme Q<sub>10</sub> percentage relative to the total coenzyme Q<sub>10</sub> contained in the composition (test sample), and the abscissa denotes the number of storage days. At 4 weeks after starting storage, the bulk powder of reduced coenzyme Q<sub>10</sub> showed a decrease in the reduced coenzyme Q percentage to 11% whereas the reduced coenzyme Q percentage was not lower than 65% in all the powder compositions I-IV.

## BEST MODES FOR CARRYING OUT THE INVENTION

The following examples elucidate the effects of the invention. These examples are, however, by no means limitative of the scope of the invention.

In the examples, a reduced coenzyme Q concentration and an oxidized coenzyme Q concentration were determined by the following HPLC analysis.

(HPLC analysis conditions)

Column; SYMMETRY C18 (product of Waters Corporation), 250 mm (length), 4.6 mm (inside diameter), mobile phase; C<sub>2</sub>H<sub>5</sub>OH : CH<sub>3</sub>OH = 4:3 (v:v), detection wavelength; 210 nm, flow rate; 1 ml/min, retention time for a reduced coenzyme Q<sub>10</sub>; 9.1 min, retention time for an oxidized coenzyme Q<sub>10</sub>; 13.3 min.

The spray drying was performed at an inlet temperature of 170°C, an outlet temperature of 80°C and a

spray rate of 100 ml/min using an Okawara Mfg. Co., Ltd. model L-12 spray drier.

(Example 1)

205 g of  $\gamma$ -cyclodextrin was dissolved in 1336 ml of  
5 water, immediately thereafter, 18 g of reduced coenzyme Q<sub>10</sub>  
(containing 2% of oxidized coenzyme Q<sub>10</sub>) was added,  
followed by 20 minutes of stirring at 10,000 rpm using a  
homogenizer so that a mixture of reduced coenzyme Q<sub>10</sub> and  
the cyclodextrin was prepared. The thus-prepared reduced  
10 coenzyme Q<sub>10</sub>-cyclodextrin mixture was subjected to spray  
drying to give a powdery composition (I). The mole  
proportions of the materials constituting this powdery  
composition were; reduced coenzyme Q<sub>10</sub> :  $\gamma$ -cyclodextrin =  
1:8.

15 (Example 2)

12.2 g of ascorbic acid was dissolved in 675 ml of  
water with thorough stirring, 85.3 g of  $\gamma$ -cyclodextrin was  
then dissolved in the solution and, immediately thereafter,  
15 g of reduced coenzyme Q<sub>10</sub> (containing 2% of oxidized  
20 coenzyme Q<sub>10</sub>) was added, followed by 20 minutes of stirring  
at 10,000 rpm using a homogenizer so that a mixture of  
reduced coenzyme Q<sub>10</sub> and the cyclodextrin was prepared. The  
thus-prepared reduced coenzyme Q<sub>10</sub>-cyclodextrin mixture was  
subjected to spray drying to give a powdery composition  
25 (II). The mole proportions of the materials constituting  
this powdery composition were; reduced coenzyme Q<sub>10</sub> :  $\gamma$ -  
cyclodextrin : ascorbic acid = 1:4:4.

(Example 3)

12.2 g of ascorbic acid was dissolved in 1188 ml of  
30 water with thorough stirring, 171 g of  $\gamma$ -cyclodextrin was  
then dissolved in the solution and, immediately thereafter,  
15 g of reduced coenzyme Q<sub>10</sub> (containing 2% of oxidized  
coenzyme Q<sub>10</sub>) was added, followed by 20 minutes of stirring  
at 10,000 rpm using a homogenizer so that a mixture of  
35 reduced coenzyme Q<sub>10</sub> and the cyclodextrin was prepared. The

thus-prepared reduced coenzyme Q<sub>10</sub>-cyclodextrin mixture was subjected to spray drying to give a powdery composition (III). The mole proportions of the materials constituting this powdery composition were; reduced coenzyme Q<sub>10</sub> : γ-cyclodextrin : ascorbic acid = 1:8:4.

(Example 4)

16.3 g of ascorbic acid was dissolved in 1182 ml of water with thorough stirring, 171 g of γ-cyclodextrin was then dissolved in the solution and, immediately thereafter, 10 g of reduced coenzyme Q<sub>10</sub> (containing 2% of oxidized coenzyme Q<sub>10</sub>) was added, followed by 20 minutes of stirring at 10,000 rpm using a homogenizer so that a mixture of reduced coenzyme Q<sub>10</sub> and the cyclodextrin was prepared. The thus-prepared reduced coenzyme Q<sub>10</sub>-cyclodextrin mixture was subjected to spray drying to give a powdery composition (IV). The mole proportions of the materials constituting this powdery composition were: reduced coenzyme Q<sub>10</sub> : γ-cyclodextrin : ascorbic acid = 1:12:8.

(Example 5 to 12, Comparative Examples 1 and 2)

Reduced coenzyme Q<sub>10</sub> bulk powder (Q-OH bulk powder) containing 2% of oxidized coenzyme Q<sub>10</sub> and the powdery compositions I to IV respectively obtained in Examples 1 to 4 were subjected to stability testing in the following manner. Thus, each composition (test sample) was placed in a microtube and stored, in a state protected against light, at 23°C or 40°C in the presence of air. The test samples used and the test temperatures are shown in Table 1.



Table 1

		Test samples	Test temperature
5	Example 5	Powdery composition (I)	23°C
	Example 6	Powdery composition (II)	23°C
	Example 7	Powdery composition (III)	23°C
	Example 8	Powdery composition (IV)	23°C
10	Comparative Example 1	Reduced coenzyme Q <sub>10</sub> bulk powder (Q-OH bulk powder)	23°C
	Example 9	Powdery composition (I)	40°C
	Example 10	Powdery composition (II)	40°C
	Example 11	Powdery composition (III)	40°C
15	Example 12	Powdery composition (IV)	40°C
	Comparative Example 2	Reduced coenzyme Q <sub>10</sub> bulk powder (Q-OH bulk powder)	40°C

After 1, 2 or 4 weeks of storage, 25 mg of each sample was sampled and dissolved in ethanol, the concentrations of oxidized coenzyme Q<sub>10</sub> and reduced coenzyme Q<sub>10</sub> were measured by HPLC and the percentage of reduced coenzyme Q<sub>10</sub> in total coenzyme Q<sub>10</sub> as contained in the composition (test sample) was determined. The results are shown in Fig. 1 and Fig. 2.

(Examples 13 to 16, Comparative Example 3)

Coenzyme Q<sub>10</sub> bulk powder (Q-OH bulk powder) containing 98% of reduced coenzyme Q<sub>10</sub> and the powdery compositions obtained in Examples 1 to 4 were subjected to solubility testing in the following manner. Thus, 1 g of each composition (test sample) was added to 100 ml of water, and the mixture was stirred at 5,000 rpm for 30 seconds using a mixer and then allowed to stand. After 1 hour of standing, the condition of the aqueous solution was observed for confirming the solubility in water. The

results are shown in Table 2.

Table 2

5		Test samples	Solubility in water
	Example 13	Powdery composition (I)	Soluble, homogeneously dispersed
10	Example 14	Powdery composition (II)	Soluble, homogeneously dispersed
	Example 15	Powdery composition (III)	Soluble, homogeneously dispersed
	Example 16	Powdery composition (IV)	Soluble, homogeneously dispersed
15	Comparative Example 3	Reduced coenzyme Q <sub>10</sub> bulk powder (Q-OH bulk powder)	Insoluble

20 Coenzyme Q<sub>10</sub> bulk powder (Q-OH bulk powder) containing 98% of reduced coenzyme Q<sub>10</sub> was insoluble, forming orange-colored oil drops floating on the water. On the contrary, the powdery compositions I to IV obtained in Examples 1 to 4 were all found to be uniformly dispersed in  
25 water in a white emulsion-like state.

#### INDUSTRIAL APPLICABILITY

The invention has made it possible to provide reduced coenzymes Q highly useful as antioxidants or nutrient  
30 supplement components in the form of compositions soluble in water and, at the same time, excellent in storage stability.